



Practitioner's Docket No. 59873 (50024)

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of: V. Manahilov

Group No.: 2851

Application No.: 10 /656,680

Filed: September 5, 2003

Examiner: Not Yet Assigned

For: SYSTEMS AND APPARATUS FOR ASSESSMENT OF VISUAL FIELD FUNCTIONS

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Country: **Great Britain**

Application Number: **0220721.5**

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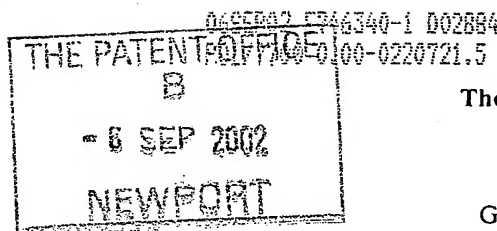
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1. Your reference

P30241-AMO/JCO

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0220721.5

- 6 SEP 2002

3. Full name, address and postcode of the or of each applicant (underline all surnames)

University Court of Glasgow Caledonian University  
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Cowcaddens Road  
Glasgow G4 0BA

Patents ADP number (if you know it)

If the applicant is a corporate body, give the country/state of its incorporation

828 4481001

United Kingdom

4. Title of the invention

"Systems and Apparatus For Assessment of Visual  
Field Functions"

5. Name of your agent (if you have one)

AgentName

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1     Systems and Apparatus for Assessment of Visual Field  
2     Functions

3

4     The present invention relates to systems, apparatus  
5     and associated methods for use in the assessment of  
6     visual field functions. In its various aspects, the  
7     invention is particularly concerned with perimetry  
8     testing and visual evoked potential (VEP) testing.

9

10    Perimetry is the systematic measurement of visual  
11    field function. It is used in diagnosing different  
12    diseases of the eye, optic nerve and central nervous  
13    system. The conventional methods for assessment of  
14    visual defects of peripheral vision are based of  
15    measurement of responses to visual stimuli presented  
16    at various locations in the visual field. Several  
17    techniques use this approach:

- 18    (i) White-on-white (W-W) perimetry detects visual  
19       field impairments by measuring the sensitivity  
20       to a small luminance target presented on a  
21       homogeneous background [ref.1]. The two most  
22       commonly used types of W-W perimetry are

1 Goldmann kinetic perimetry and threshold static  
2 automated perimetry. With Goldmann or "kinetic"  
3 perimetry, a trained perimetrist moves the  
4 target whose brightness is held constant. The  
5 limits of the visual field are mapped for  
6 targets of different sizes and brightness. With  
7 threshold static automated perimetry, a  
8 computer program is used to vary the target  
9 brightness until the dimmest target the patient  
10 can see at each of the test locations is found.  
11 The data are used to construct a map of the  
12 visual sensitivity of the retina.

13 (ii) Short wavelength automated perimetry (SWAP)  
14 utilises a blue stimulus to preferentially  
15 stimulate the blue cones. A high luminance  
16 yellow background is used to adapt the green  
17 and red cones and to saturate, simultaneously,  
18 the activity of the rods.

19 (iii) Frequency-doubling perimetry (FDP) uses  
20 rapidly flickering gratings. These stimuli  
21 create an illusion (apparent doubling of  
22 grating spatial frequency) that allows only a  
23 small set of retinal ganglion (M cells) cells  
24 to respond.

25

26 These techniques reveal visual defects by comparing  
27 patients' results with those obtained with normal  
28 observers. A disadvantage of these approaches is  
29 that visual sensitivity is measured by  
30 psychophysical procedures which usually depend on  
31 the criterion used by the observers. This might

1 result in large inter-individual differences which  
2 reduce the sensitivity of the measurements.

3 Objective techniques have also been developed:

4 (i) Multifocal electroretinogram (ERG) perimetry.

5 ERGs are electrical signals generated by  
6 retinal cells in response to a visual stimulus.  
7 MERGs are elicited by a pseudorandom binary m-  
8 sequence of luminance patches. The luminance of  
9 each sector of a dartboard-like pattern  
10 alternates between white and black. MERGs  
11 elicited by different patches are analysed by a  
12 reverse correlation technique in order to  
13 construct a map of the responses of retinal  
14 cells.

15 (ii) Multifocal visual evoked potential (VEP)

16 perimetry. VEPs are electrical signals  
17 generated by cortical cells in response to a  
18 visual stimulus. The stimulation is also based  
19 on a pseudo-random binary m-sequence of visual  
20 targets presented in different visual-field  
21 locations. A reverse correlation technique is  
22 used to analyse the data.

23

24 It is known that the visual cortex has an expanded  
25 representation of the fovea because of the high  
26 density of ganglion cells in the fovea. The fovea is  
27 represented on the surface of the brain. The  
28 activity of this area can be recorded by scalp  
29 electrodes. The primary visual cortex representing  
30 the peripheral parts of the visual field, however,  
31 is folded in deeper areas of the brain. These areas

1 of the primary visual cortex contribute little to  
2 the VEPs.

3

4 One aspect of the present invention concerns long-  
5 distance perimetry, providing new systems, apparatus  
6 and associated methods for assessment of visual-  
7 field defects which are based on measurement of  
8 long-distance interactions between an "inducing"  
9 stimulus and a "test" stimulus.

10

11 The term "long-distance interactions" usually refers  
12 to interactions between the responses to two stimuli  
13 whose separation is larger than the receptive field  
14 size. Electrophysiological studies have shown that  
15 the responses of cells in cat and monkey retina,  
16 lateral geniculate nucleus and visual cortex can be  
17 affected by a moving or shifting luminance pattern  
18 outside their receptive fields [refs.2-5].

19 Psychophysical data also have shown that the  
20 threshold visibility of a foveal test spot was  
21 reduced when a luminance grating is jerked in the  
22 periphery of the visual field [refs.6-8].

23 Measurements of visual evoked potentials (VEPs) in  
24 humans have demonstrated that the contrast reversal  
25 of a structured image reduced the magnitude of the  
26 VEPs elicited by a foveal stimulus [ref.9].

27

28 One possible explanation of these findings is that  
29 long-distance interactions between the peripheral  
30 inducing stimulus and the test stimulus may increase  
31 the neural internal noise of the cells which are  
32 involved in the detection of the test pattern

1 [ref.8]. The increased internal noise will require a  
2 stronger signal in order to maintain a given level  
3 of visibility. Another possible explanation is based  
4 on the assumption that the long-distance  
5 interactions result in cortical transient-to-  
6 sustained neurone inhibition [ref.8].

7  
8 One aspect of the present invention uses the  
9 phenomenon of long-distance interactions as a  
10 perimetric tool. In essence, a flashing peripheral  
11 stimulus reduces the response to a central test spot  
12 if the peripheral location has normal functioning.  
13 Lack of effect points to a loss of visual function  
14 at the peripheral location. The long-distance effect  
15 is estimated by methods of psychophysics and visual  
16 evoked potentials.

17  
18 In accordance with a first aspect of the invention,  
19 there is provided apparatus for use in the  
20 assessment of visual field functions, comprising:

21 a visual display device adapted to display  
22 visual stimulus patterns; and

23 a computer adapted to generate visual stimulus  
24 patterns within a predetermined visual field and to  
25 control the display of said visual stimulus patterns  
26 by said visual display device; wherein:

27 said computer is adapted to generate a test  
28 stimulus for display in a central region of the  
29 visual field and to generate an inducing stimulus  
30 for display in a peripheral region of the visual  
31 field, and to control the visual display device so  
32 as to selectively display the test stimulus alone

1 and in combination with the inducing stimulus in  
2 accordance with a predetermined test protocol.

3  
4 Preferably, the visual display device is a plasma  
5 monitor.

6  
7 In embodiments for use in electrophysiological  
8 testing, the apparatus preferably further includes:  
9 at least three test electrodes for detecting  
10 VEPs in response to visual stimuli displayed by said  
11 display device; and

12 a computer adapted to record VEP signals from  
13 said test electrodes and to compare VEP signals  
14 generated in response to the display of the test  
15 stimulus alone with VEP signals generated in  
16 response to the display of the test stimulus in  
17 combination with the inducing stimulus.

18  
19 Preferably, the computer is adapted to calculate a  
20 Laplacian response (second spatial derivative) from  
21 each set of VEP signals and to calculate a ratio of  
22 the Laplacian response for the test stimulus alone  
23 and the Laplacian response for the combination of  
24 the test stimulus and inducing stimulus.

25  
26 In embodiments for use in psychophysical testing,  
27 the apparatus preferably further includes:  
28 control means operable by a test subject for  
29 increasing and decreasing the contrast of the visual  
30 stimulus displayed by the display device and for  
31 indicating a threshold contrast value.

32

1 Preferably, the computer is adapted to execute a  
2 test protocol comprising: generating a first visual  
3 stimulus; recording a first threshold contrast value  
4 indicated by the test subject using the control  
5 means; displaying the stimulus again with a contrast  
6 equal to a randomly selected multiple of the first  
7 threshold contrast; recording a second threshold  
8 contrast value indicated by the test subject using  
9 the control means; repeating this process for a  
10 predetermined number of iterations; and calculating  
11 a mean threshold contrast value from said first,  
12 second and subsequent threshold contrast values.

13

14 Preferably, the computer is adapted to calculate a  
15 mean threshold value for a stimulus comprising the  
16 test stimulus alone and a stimulus comprising the  
17 combination of the test stimulus and inducing  
18 stimulus, and to calculate the ratio of these two  
19 mean threshold values.

20

21 In accordance with a second aspect of the invention,  
22 there is provided a method for assessing visual  
23 field functions, comprising:

24 displaying visual stimulus patterns within a  
25 predetermined visual field using a visual display  
26 device, said visual stimulus patterns comprising a  
27 test stimulus displayed in a central region of the  
28 visual field and an inducing stimulus displayed in a  
29 peripheral region of the visual field; and  
30 selectively displaying the test stimulus alone and  
31 in combination with the inducing stimulus in  
32 accordance with a predetermined test protocol.

1  
2 Preferably, the visual display device is a plasma  
3 monitor.

4  
5 In embodiments for use in electrophysiological  
6 testing, the method preferably further includes:  
7       deploying at least three test electrodes for  
8 detecting VEPs in response to visual stimuli  
9 displayed by said display device; and  
10       recording VEP signals from said test electrodes  
11 and comparing VEP signals generated in response to  
12 the display of the test stimulus alone with VEP  
13 signals generated in response to the display of the  
14 test stimulus in combination with the inducing  
15 stimulus.

16  
17 Preferably, the method includes calculating a  
18 Laplacian response (second spatial derivative) from  
19 each set of VEP signals and calculating a ratio of  
20 the Laplacian response for the test stimulus alone  
21 and the Laplacian response for the combination of  
22 the test stimulus and inducing stimulus.

23  
24 In embodiments for use in psychophysical testing,  
25 the method preferably further includes:

26       the test subject operating control means to  
27 increase and decrease the contrast of the visual  
28 stimulus displayed by the display device and to  
29 indicate a threshold contrast value.

30  
31 Preferably, the method includes a test protocol  
32 comprising: generating a first visual stimulus;

1 recording a first threshold contrast value indicated  
2 by the test subject using the control means;  
3 displaying the stimulus again with a contrast equal  
4 to a randomly selected multiple of the first  
5 threshold contrast; recording a second threshold  
6 contrast value indicated by the test subject using  
7 the control means; repeating this process for a  
8 predetermined number of iterations; and calculating  
9 a mean threshold contrast value from said first,  
10 second and subsequent threshold contrast values.

11

12 Preferably, the method further includes calculating  
13 a mean threshold value for a stimulus comprising the  
14 test stimulus alone and a stimulus comprising the  
15 combination of the test stimulus and inducing  
16 stimulus, and calculating the ratio of these two  
17 mean threshold values.

18

19 In accordance with a third aspect of the invention,  
20 there is provided apparatus for use in the  
21 assessment of visual field functions, comprising:

22 a visual display device adapted to display  
23 visual stimulus patterns;

24 a computer adapted to generate visual stimulus  
25 patterns within a predetermined visual field and to  
26 control the display of said visual stimulus patterns  
27 by said visual display device, said computer being  
28 adapted to generate test stimuli for display in a  
29 first region of the visual field and to generate  
30 visual Gaussian noise patterns of different noise  
31 densities for display in at least one other region  
32 of the visual field, and to control the visual

1 display device so as to selectively display the test  
2 stimulus alone and in combination with the noise  
3 pattern in accordance with a predetermined test  
4 protocol;

5 at least three test electrodes for detecting  
6 VEPs in response to visual stimuli displayed by said  
7 display device; and

8 a computer adapted to record VEP signals from  
9 said test electrodes, to calculate a Laplacian  
10 response (second spatial derivative) from each set  
11 of VEP signals, and to derive an internal neural  
12 noise value for said first region of the visual  
13 field from said Laplacian responses and associated  
14 Gaussian noise densities.

15

16 In accordance with a fourth aspect of the invention,  
17 there is provided a method for assessing visual  
18 field functions, comprising:

19 generating visual stimulus patterns within a  
20 predetermined visual field using a visual display  
21 device, said stimulus patterns comprising test  
22 stimuli displayed in a first region of the visual  
23 field and visual Gaussian noise patterns of  
24 differing noise densities displayed in at least one  
25 other region of the visual field; and selectively  
26 displaying the test stimulus alone and in  
27 combination with the noise pattern in accordance  
28 with a predetermined test protocol;

29 deploying at least three test electrodes for  
30 detecting VEPs in response to visual stimuli  
31 displayed by said display device; and

1           recording VEP signals from said test  
2   electrodes, calculating a Laplacian response (second  
3   spatial derivative) from each set of VEP signals,  
4   and deriving an internal neural noise value for said  
5   first region of the visual field from said Laplacian  
6   responses and associated Gaussian noise densities.

7  
8   Embodiments of the invention will now be described,  
9   by way of example only, with reference to the  
10   accompanying drawings, in which:

11  
12   Fig. 1 is a diagram illustrating one example of the  
13   type of visual stimuli employed in embodiments of  
14   the present invention; and

15  
16   Fig. 2 is a block diagram illustrating apparatus in  
17   accordance with one embodiment of the present  
18   invention.

19  
20   Referring now to the drawings, Fig. 1 shows one  
21   example of the type of stimuli used for the purposes  
22   of the invention. The drawing illustrates the  
23   visual field as a circular dartboard pattern, with  
24   an "inducing stimulus" I comprising a series of  
25   concentric circles around the periphery of the field  
26   and a "test stimulus" T comprising a circular visual  
27   checkerboard or noise pattern at the centre of the  
28   field. It will be understood that the nature of  
29   these stimuli may vary widely. In particular, the  
30   inducing stimulus I may vary in terms of its  
31   location within the visual field, the type of  
32   pattern and the dynamics of the stimulus (generally,

1 the stimuli will comprise time varying patterns,  
2 typically including flashing or contrast reversal at  
3 a particular frequency). The stimuli are discussed  
4 further below.

5  
6 The stimuli are generated by a first computer 10  
7 (Fig. 2) and presented by means of any suitable  
8 visual display apparatus 12. The visual display  
9 apparatus 12 may comprise any of a variety of well  
10 known display devices, including cathode ray tubes,  
11 LCD displays, video projectors etc. It is preferred  
12 that the display area is relatively large in order  
13 to allow a reasonable distance between the test  
14 subject and the display. It is particularly  
15 preferred that the display 12 comprises a plasma  
16 type monitor, which provides a large display area  
17 and instantaneous screen updates (as compared with  
18 raster-scan type displays).

19  
20 As noted above, the first computer 10 generates the  
21 stimuli and controls the display apparatus 12. When  
22 the invention is applied for electrophysiological  
23 testing, the apparatus further includes a second  
24 computer 14, connected to electrodes 16 for  
25 detecting the subject's neural responses, which  
26 records and processes signals from the electrodes  
27 16, as described further below. The first and  
28 second computers 10 and 14 are connected to enable  
29 the correlation of stimuli and responses.  
30 Alternatively, the functions of the first and second  
31 computers may be performed by a single computer or  
32 by any other suitable arrangement of computers.

1  
2 When the invention is applied for psychophysical  
3 testing, as also described further below, the second  
4 computer 14 and electrodes 16 are not required, and  
5 the apparatus further includes a control unit 18  
6 connected to the first computer 10 and operable by  
7 the test subject.

8  
9 In this example, the inducing stimulus I comprises a  
10 circular grating presented in a peripheral sector of  
11 the visual field as shown in Fig. 1. This stimulus  
12 will be flickering or moving. The test stimulus T  
13 may be a checkerboard or visual noise pattern  
14 flickering at F Hz.

15  
16 The invention may be applied for  
17 electrophysiological testing by recording monopolar  
18 VEPs elicited by the test stimulus using at least  
19 three test electrodes attached on the skin, suitably  
20 in a transverse row across the occiput, e.g. at  
21 locations O3, Oz and O4 (standard nomenclature for  
22 locations on the skull), plus (preferably) a  
23 reference electrode, e.g. attached at location Fz.  
24 The VEPs from the test electrodes are used to  
25 calculate the second spatial derivative of the  
26 potential field distribution (Laplacian responses)  
27 [refs. 10-11]. The Laplacian response, L, may be  
28 calculated for example, as

$$29 \quad L = 2Oz - O4 - O3.$$

30  
31 The generators of the early component of the  
32 Laplacian responses are located within the primary

1 visual cortex. Laplacian responses have several  
2 advantages as compared to monopolar VEPs. They have  
3 higher signal-to-noise ratio; they do not depend on  
4 the reference electrode; alpha activity and  
5 electrical signals due to eye movements are  
6 eliminated. The Laplacian responses may be  
7 recognised in a single sweep [ref. 13].

8  
9 The Laplacian responses elicited by the test  
10 stimulus T are recorded in absence and presence of  
11 the inducing stimulus I. The Laplacian responses are  
12 attenuated due to long-distance interactions in the  
13 visual network. The presence of defects in the area  
14 where the inducing stimulus I is displayed might  
15 result in a reduced inducing effect. The ratio  
16 between the Laplacian responses to the test stimulus  
17 T in the absence and presence of the inducing  
18 stimulus I can be used to evaluate visual defects in  
19 the area where the inducing stimulus I is presented.  
20 If the stimulated peripheral area has normal  
21 functions, the Laplacian ratio will be less than 1  
22 (i.e. the response to the test stimulus T is  
23 affected by the presence or absence of the inducing  
24 stimulus I). If the stimulated peripheral area has a  
25 visual defect, the Laplacian ratio will be 1 (i.e.  
26 the response to the test stimulus T is not affected  
27 by the presence or absence of the inducing stimulus  
28 I).

29  
30 The second computer 14 is adapted and programmed to  
31 record the signals from the electrodes 16 and to  
32 process the signals as described above.

1  
2 When the invention is applied for psychophysical  
3 testing, the contrast threshold for detection of the  
4 test stimulus T is measured by the method of  
5 adjustment. The test subject has to fixate the  
6 centre of the display 12. Two buttons on the control  
7 unit (or "response box) 18 enable the subject to  
8 decrease and increase the stimulus contrast. Using  
9 these buttons the subject varies the contrast until  
10 a just noticeable sensation of flicker occurs.  
11 Pressing a third button then indicates that the  
12 threshold contrast has been reached and the computer  
13 10 will record its value. The stimulus then appears  
14 again, but its contrast is randomly selected by the  
15 computer 10 to be a multiple (suitably 3-10 times  
16 higher or lower) of the measured threshold contrast.  
17 The programme repeats the measurements until a  
18 suitable number (e.g. 10) thresholds are collected  
19 for each experimental condition.  
20  
21 The mean threshold is determined in the absence and  
22 presence of the inducing stimulus. The ratio between  
23 these two mean threshold measurements may be used  
24 for assessment of visual defects in the area where  
25 the inducing stimulus is presented, e.g. in a  
26 similar manner to that described above for  
27 electrophysiological testing.  
28  
29 In summary, long-distance perimetry in accordance  
30 with the present invention is based on interactions  
31 between the responses to an inducing stimulus I and  
32 a test stimulus T. The magnitude of visual defects

1 in the early stages of the visual system is  
2 evaluated by the ratio between the responses to the  
3 test stimulus T in the absence and presence of the  
4 inducing stimulus I. This relative measurement will  
5 reduce inter-individual differences, as compared  
6 with conventional methods based on "absolute  
7 sensitivity" measurements.

8  
9 The psychophysical test as described above may be  
10 applied for patients who can understand and perform  
11 the visual task. The electrophysiological test is an  
12 objective procedure which requires only fixation at  
13 the centre of the display.

14  
15 According to another aspect, the invention may also  
16 be applied for the purpose of measuring internal  
17 neural noise. Internal noise may be associated with  
18 neural fluctuations of early visual stages [ref. 12].  
19 The method of visual evoked potentials (VEPs) in the  
20 presence of external noise [ref. 13] may be used to  
21 evaluate internal noise at different retinal areas.

22  
23 In this case the stimuli presented by the display  
24 apparatus 12 consist of test patterns presented at  
25 various parts of the retina/visual field. Laplacian  
26 responses are recorded without noise and in the  
27 presence of several densities of external Gaussian  
28 dynamic noise, N. Thresholds are estimated from the  
29 contrast-axis intercept of linear regression  
30 approximating the contrast response; i.e. if the VEP  
31 response is plotted as a function of contrast, the  
32 intercept with the contrast-axis (zero response)

1 indicates the threshold contrast. The threshold  
2 signal energy is approximately equal to the threshold  
3 contrast squared, multiplied by a constant.

4 Threshold signal energy  $E$  as a function of external  
5 noise density is fitted by equation (1):

$$6 \quad E = (N + N_i) / G \quad (1)$$

7 The intercept on the noise density axis,  $N_i$ , is the  
8 equivalent input noise that is a measure of the  
9 internal noise. The slope is a measure of the  
10 response gain  $G$ .

11  
12 The results provide objective information about  
13 internal noise and response gain of different parts  
14 of the retina.

15  
16 Improvements and modifications may be incorporated  
17 without departing from the scope of the invention.

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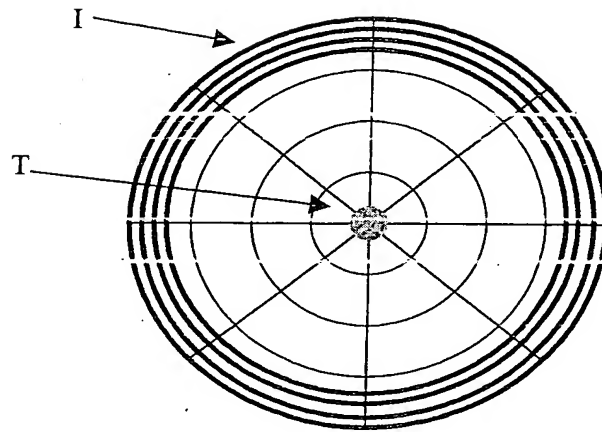


Fig. 1

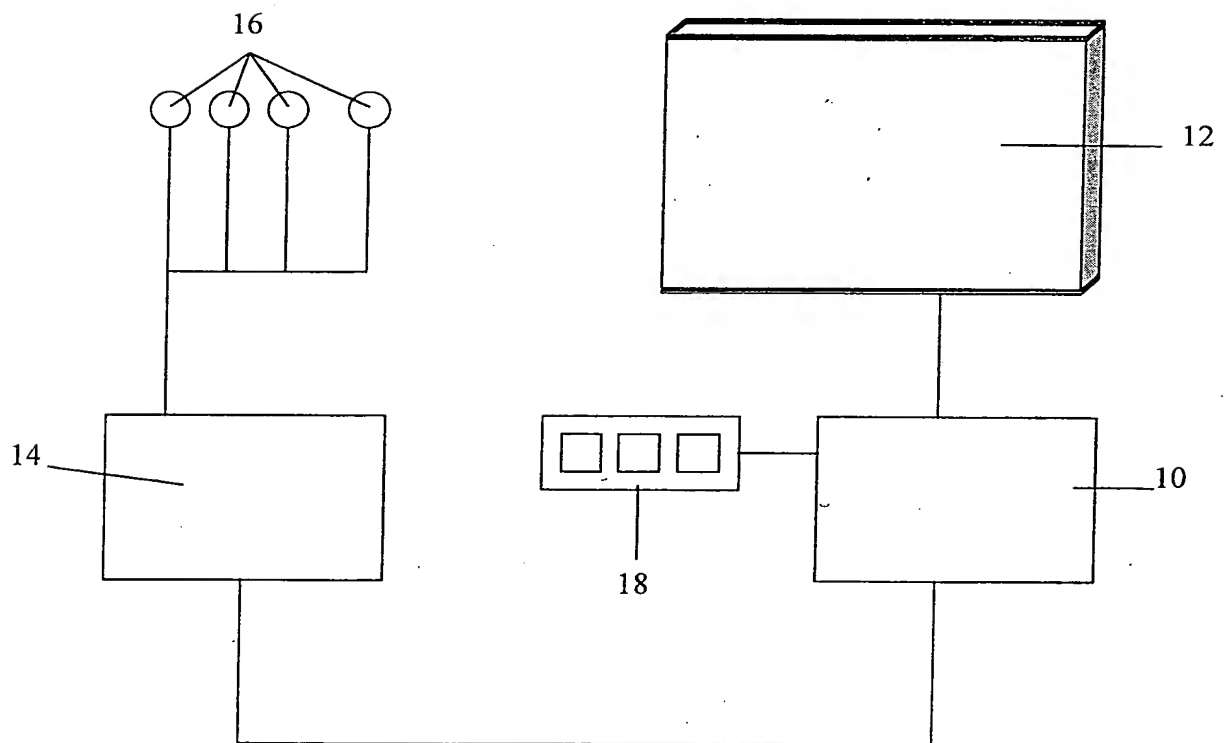


Fig.2



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